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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,810	03/21/2001	Richard Anthony Flynn	21025-11	8199

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EXAMINER
BENNETT, RACHEL M

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 04/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,810	FLYNN ET AL.	
	Examiner	Art Unit	
	Rachel M. Bennett	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,15-19,22 and 26-28* is/are rejected.

7)☒ Claim(s) *8-14,20,21 and 23-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner acknowledges receipt of the Information Disclosure Statement filed 6/7/01.

Specification

1. Applicant is advised that should claims 1-3, 15 be found allowable, claim 22, 26-28 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objections

2. Claims 8-14, 20-21, 23-25 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend form any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 8-14, 20-21, 23-25 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7, 15-19, 22, 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-7, 15-19, 22, 26-28 are indefinite because Applicants do not clearly define the diameter of micronised particles. The instant claims read "a diameter of less than 10 micrometers". Thus, including zero. It is suggested, Applicants indicate a lower range for the particle size.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 1-7, 15-19, 22, 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US 5641510), and further in view of Rose et al. ("Evaluation of Sodium Colistmentate Aerosol") and Catchpole et al. ("A reassessment of in-virtto activity of colistin sulphomethate sodium").

Clark discloses capsules (such as hard gelatin, cellulose and plastic capsules) containing pharmaceutical powders which are administered to a patient via inhalation are treated so as to increase the effective amount of the pharmaceutical agent reaching the respiratory system of the patient. The capsules are coated internally with a lubricant during manufacture. The lubricant-coated capsule is dusted internally with a dusting agent such as a salt (e.g. sodium chloride) or a sugar (e.g. lactose, mannitol, trehalose or sucrose) prior to inserting the pharmaceutical powder inside the capsule (see abstract). This method serves to improve aerosol delivery of the pharmaceutical powder to the patient. The term "pharmaceutical powder" refers to a powder containing at least a pharmaceutical compound and, optionally, a pharmaceutical acceptable carrier or excipient. The pharmaceutical powder is generally administered to the respiratory tract of the patient in the form of an aerosol. Examples of pharmaceutical compounds which might usefully be incorporated into the hard gelatin capsule include pharmaceutical polypeptides, anti-bacterials and antibiotics (see cols. 5 and 6). A mixture of pharmaceutically compound particles

and an excipient can form the pharmaceutical powder. Examples of pharmaceutically acceptable carriers or excipients include, but are not limited to, salt compounds (e.g. sodium chloride) or sugar compounds (e.g. glucose, fructose, lactose, mannitol, trehalose and sucrose). Other conventional agents such as those which are conventionally incorporated into dry powder inhalant compositions may be present in the pharmaceutical powder. The average particle size of the particles of the pharmaceutical powder containing the therapeutic agent is preferably in the range 0.1 to 20 micrometers, more preferably 1 to 6 micrometers. Typically, at least 50% of the particles will be of a size which falls within this range, although the presence of significant quantities of fine material is contemplated within the scope of the invention (see col. 5 lines 1-13). The pharmaceutical powder having the desired particle average particle size can be prepared by dry mixing the pharmaceutical compound and the excipient. Clark does not teach the antibiotic to be colistin sulphomethate sodium.

Rose discloses the evaluation of sodium colistimethate aerosol in gram-negative infections of the respiratory tract. Sodium colistimethate (SCM), the methane sulfonate derivative of colistin, is bacterial and active against many strains of gram-negative bacilli. SCM is used for aerosol therapy, dissolved in sterile water and administered by intermittent positive pressure breathing instruments yielding a particle size of 1-7 microns. SCM in aerosol form is well tolerated by all patients except one, who in addition to obstructive pulmonary disease, suffered from angina pectoris. Daily dosages ranging from 75 to 300 mg, given one to three times a day, given one to three times a day, resulted in pathogen free sputum cultures in 60% of the patients. The results of the study indicate that aerosolized SCM is well tolerated and

effective in eradicating or suppressing susceptible gram-negative organisms carried in the respiratory tract of patients with underlying pulmonary disease.

Catchpole discloses a reassessment of in-vitro activity of colistin sulphomethate sodium. Colistin is known to be used as inhaled therapy for treatment of infection by *Pseudomonas aeruginosa* in patients with cystic fibrosis. The in-vitro activity of colistin sulphomethate sodium was compared with that of other commonly used antibiotic agents against 377 recent clinical isolates of Gram-negative bacterial, including 94 strains of *Pseudomonas aeruginosa* from patients with cystic fibrosis. The results show that colistin remains a useful antimicrobial agent against Gram-negative bacteria, particularly those strains which are resistant to more commonly used antibiotics (see abstract).

Absent unexpected results, it would have been obvious to one of ordinary skill in the art at the invention was made to have modified the composition of Clark by substituting colistin sulphomethate sodium as taught by Rose and Catchpole for the antibiotic taught by Clark because of the expectation of producing an composition that is "well tolerated and effective in eradicating or suppressing susceptible gram-negative organisms carried in the respiratory tract of patients with underlying pulmonary disease" as taught by Rose and provide an added advantage of "a useful antimicrobial agent against Gram-negative bacteria, particularly those strains which are resistant to more commonly used antibiotics" as taught by Catchpole. Colistin sulphomethate sodium is known to be in micronised particles as taught by Rose. Therefore, the expected result would be micronised particles, with the desired diameter mixed with a carrier in the desired ratio of colistin sulphomethane sodium to carrier.

Art of Interest

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Simpkin (GB 2269992 A) discloses a powder composition for inhalation comprising at least one microfine drug and a carrier. Dodd et al. (Thorax) disclose effect of tonicity of nebulised colistin on chest tightness and pulmonary function in adults with cystic fibrosis. Rogers et al. discloses a comparison of the binding of gram-negative bacterial endotoxin by polymyxin B sulphate, colistin sulphate and colistin sulphomethate sodium. VanDevanter et al. (US 5767068) discloses colistin, it components and mixtures thereof delivered as an aerosol or dry powder formulation.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 309-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

R. Bennett: RMB RMB
April 5, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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